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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/066,157
Filing Date: January 31, 2002
Appellant(s): CORSON, JOHN F.

Bret Field
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 12/13/05 appealing from the Office action mailed 6/15/05.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

WO 99/47964	Overbeck	9-1999
5,812,272	King et al.	9-1998

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims **15-21, 27, 29-30, 33-37, 39-45** and **47-48** are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/47964. to Overbeck.

WO '964 teaches a wide angle, limited rotation, micro-lens scanning of DNA arrays. The micro-lens on low moment of inertial oscillating arm, while light source 24, detector 10,95, and supplementary lenses are stationary, achieve rapid, wide angle pixel-based microscopy. Auto focus raising and lowering stage 50, by actuator 44, while object 2 translates, enables rapid, wide-angle confocal microscopy (abstract). The scanning microscope includes a light source mounted on a stationary support and associated with optical elements defining an optical path for light to pass from the light source to the micro objective lens, then to a spot on the surface to be examined. In any of the microscope systems which employ a table to receive the object, the table is associated with three adjustable elevators to raise, lower, and tilt the table for focusing, and a control system is constructed to conduct a prescan of the object in which data

concerning orientation is stored, and a control system responsive to the stored data is effective to actuate the elevators as scanning proceeds to maintain the object in focus (page 14 bottom to page 15 top). All optical elements cooperate to perform in a manner similar to a conventional multi element objective lens. Starting on page 28 and continuing to page 31, the reference discloses a method of adjustment of focus of the scanner. The focus correction is detected by photosensors 10 detecting modulation of the light by the tissue sample or by fiducial points. As the tissue sample approaches perfect focus, the amplitude of the high frequency components in the signal of the photosensors is increased relative to that of the lower frequency components and best focus is defined as that height of the microscope slide at which the ratio of high frequency components to low frequency components is maximized (page 30). Prescan of the microscope slide enables determination of the height of best focus of the microscope slide at a chosen grid of points on the microscope slide. This enables detection of whether the slide is tilted or bowed. This information is stored in computer memory and accessed during the progress of the subsequent fine resolution "examination" scan. During the examination scan the microscope slide is held on its support in exactly the same position it occupied in the prescan. When the examination scan occurs, the focus mechanism continually tracks the surface of the microscope slide in accordance with the stored data. In regard to gross height error due to pitch, roll or bow the computer program analyzes the prescan data and determines gross tilt correction. The actuators are accordingly set to correct gross tilt prior to the examination scan. During examination scan, as the linear stage 11 moves gradually

while the microscope slide is scanned repeatedly, the position of the microscope slide is continually adjusted by focus mechanisms 8 based upon the stored prescan data for pitch and bow (page 31). WO '964 further discloses reading of fluorescence by conventional FITC labeling, by illuminating the objects with light of about 494 nm and collecting the low intensity fluorescing radiation of about 518 nm, the emitted light being separated from the excitation light with filters (page 40). The high numerical aperture provides excellent collection of fluorescent light that is sent in all directions by the illuminated spot (page 40). Seen in fig. 3 the light source is coplanar to the calibration member (uniform fluorescent layer). Fluorescence detection further comprises techniques for DNA sequencing where rectangular arrays of sites at which hybridization reaction occurs between a known DNA fragment and an unknown DNA (page 42). The scans are performed over very large areas because different reactions are distributed over on microscope slide (page 42).

Overbeck does not teach calibration of the focal length with a fluorescent member.

Overbeck, however does teach pre-scan of the microscope slide using a chosen grid of points on the microscope to calibrate the focal length. Overbeck further teaches that measurements are made using fluorescent detection. It would have been obvious to one of ordinary skill to prescan the slide using a fluorescent grid in order to calibrate with the same type of light being detected during measurement. As to a uniform layer versus a grid of points, it would have been obvious to employ an expanded grid to

provide the most optimum picture of the slide during pre-scan in order to provide the most accurate adjustment of the focal length during analysis.

Claims **38** and **46** are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/47964 in view of King et al. (USPN 5,812,272).

WO '964 teaches a wide angle, limited rotation, micro-lens scanning of DNA arrays as seen above.

WO '964 does not teach using CY3 and CY5 as fluorescent labels.

King teaches examples of suitable labels than can be used for fluorescent labels that include well known and commonly available ones such as fluorescenin, indocarbocyanin dyes, (e.g., CY3, CY5), Texas Rd, ethidium bromide, and chelated lanthanides (col. 8, lines 8-12). Therefore, it would have been obvious to one having an ordinary skill in the art to modify WO '964 to include CY3 and CY5 fluorescent labels because it is well known in the art to use such labels in fluorescent detection methods.

(10) Response to Argument

Claims 39-42

The Appellant argues, "Overbeck fails to teach the elements of the Appellant's invention wherein at least one sensitivity setting of the detection systems is calibrated from the calibration signals generated from the calibration member when positioned at the focal plane of the detection systems." The Examiner points to page 30-31 of

Overbeck for the main teaching of this limitation. Prescan of the microscope slide enables determination of the height of best focus of the microscope slide at a chosen grid of points on the microscope slide. This enables detection of whether the slide is tilted or bowed. This information is stored in computer memory and accessed during the progress of the subsequent fine resolution "examination" scan. During the examination scan the microscope slide is held on its support in exactly the same position it occupied in the prescan. When the examination scan occurs, the focus mechanism continually tracks the surface of the microscope slide in accordance with the stored data. Overbeck specifically states in the embodiments described, it is preferred that some adjustments be made dynamically and some not. During examination scan, as the linear stage 11 moves gradually while the microscope slide is scanned repeatedly, the position of the microscope slide is continually adjusted by focus mechanisms 8 based upon the stored prescan data for pitch and bow (page 31).

The Appellant points to page 15, lines 24-28, where no mention of definition of a sensitivity setting is mentioned. The only mention of calibration with respect to the sensitivity of the detectors is mentioned on page 16, lines 1-3, where the Appellant states, "Calibration may be accomplished by adjusting the sensitivity of detectors 150a, 150b (such as adjusting voltage in a PMT) or by adjusting gain in any attached amplifier circuit (not shown)." The Examiner relies on the broadest interpretation of calibration of a sensitivity setting and determines that adjusting for perfect focus throughout the prescan and continually adjusting the position of the microscope slide under the examination scan based upon the stored prescan data for pitch and bow teaches the

limitation of adjusting a sensitivity setting in the detection system. In other words, any change in an adjustment (focal plane) that will change how the detection system receives an emitted light from the microscope slide is interpreted as calibrating at least one sensitivity setting of the detection system. Therefore, the Examiner respectfully disagrees with the Appellants statement, "pre-scanning a microscope slide to adjust for best focus is very different from calibrating at least one sensitivity setting as claimed in Appellant's invention."

Claims 1-6, 18-21, 27, 33-37 and 43-45

The Appellant states, "Overbeck fails to teach or suggest calibrating at least one sensitivity of the detection system from the calibration signals generated from the calibration member." The Examiner would like to cite from claim 15, the correct claim language, "d) calibrating a sensitivity of the detection system form the detection system signals generated from the calibration member." The Examiner respectfully disagrees with the Appellant's position as seen in the arguments presented and directed to claims 39-42.

In addition the Appellant argues, "the Examiner has provided no citation in Overbeck that teach or suggests a calibration member having a uniform fluorescent layer." The Appellant states, "Indeed, the prescanning disclosed by Overbeck is of the slide itself (which is comprised of unevenly distributed fluorescent moites, e.g., fluorescent probes associated with the features of the array) and not of a calibration member with a uniform fluorescent layer." The Examiner has search through Overbeck

and cannot reference where the Appellant states that Overbeck's slide is comprised of unevenly distributed fluorescent moites, e.g., fluorescent probes associated with features of the array. Overbeck teaches pre-scan of the microscope slide using a chosen grid of points on the microscope to calibrate the focal length. Overbeck further teaches that measurements are made using fluorescent detection. It would have been obvious to one of ordinary skill to prescan the slide using a fluorescent grid in order to calibrate with the same type of light being detected during measurement. As to a uniform layer versus a grid of points, it would have been obvious to employ an expanded grid to provide the most optimum picture of the slide during pre-scan in order to provide the most accurate adjustment of the focal length during analysis.

Claim 17

The Appellant argues, "Overbeck neither teaches nor suggests that the light emitted from the slide is the same from each of the detection regions." The Examiner respectfully disagrees with this statement. The focus correction is detected by photosensors 10 detecting modulation of the light by the tissue sample or by fiducial points. As the tissue sample approaches perfect focus, the amplitude of the high frequency components in the signal of the photosensors is increased relative to that of the lower frequency components and best focus is defined as that height of the microscope slide at which the ratio of high frequency components to low frequency components is maximized (page 30).

Claims 29 and 47

The Appellant argues, "the Examiner has failed to cite any passage in Overbeck that teaches or suggest communication data from reading the array to a remote location." The Examiner points to page 38 of Overbeck, "Then the data is...or sent over a wide band-width communication link which may be a satellite link to a physician on the other side of the world, or by data line to another location in the same hospital or facility, or to a patient's permanent medical record." (lines 11-17).

Claims 30 and 48

The Appellant argues, "Overbeck neither teaches nor suggest a method of receiving data representing a result of a reading obtained by the methods of claim 30 or 48." Overbeck teaches that above limitation as seen on page 38 lines 11-17.

Claims 38 and 46

The Appellant argues, "However, the Appellant submits that King et al. fail to remedy the fundamental deficiencies of Overbeck as discussed in detail above. Namely, King et al. does not teach or suggest calibrating at least one sensitivity of the detection system from the calibration signals generated from the calibration member and providing a uniform fluorescent layer on the calibration member, much less a uniform fluorescent layer comprising both Cy3 and Cy5." In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references.

See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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